

Isoniazid hepatitis: are immunological mechanisms implicated?

To the editor,

Isoniazid is an antibiotic bactericidal against *Mycobacterium tuberculosis*. Initially, it was believed to be free of serious side effects, but it has potential to cause serious hepatotoxicity. Up to 20% of patients experience mild liver injury which is usually subclinical and self-limited. A less common form is Isoniazid hepatitis, a more serious syndrome of liver injury that may be fatal. Age is an important risk factor (rare in persons younger than 20 years). Other risk factors are alcohol, use of medications that induce CYP P450¹, chronic viral hepatitis, and being female. Most cases occur within the first two to three months after initiation of therapy. The mechanism of liver damage is not completely understood, although it seems related to direct toxicity of the drug or a metabolite. Acetylators status may also be implicated². There is no evidence so far that allergy or other hypersensitivity reactions play a role³.

A 21-year-old female patient with tuberculosis presented with fever, abdominal pain, generalised rash with sloughing and elevation of liver enzymes after two weeks of treatment with Isoniazid, Pyrazinamide and Rifampicin. Systemic corticosteroids and antihistamines were administered and the drugs were withdrawn.

Epicutaneous test with the implicated drugs were performed (pure and diluted 1/10 with DMSO and vaseline). Five negative healthy controls were performed.

Late readings at two and four days showed positive results to Isoniazid (Figure 1). Pyrazinamide and Rifampicin were negative. Five negative healthy controls were performed. An oral single-blind placebo controlled trial with Rifampicin and Pyrazinamide proved negative.

Alternative regimen without Isoniazid was established, with total recovery of liver function.

We report a rare case of hepatitis with skin implication selectively caused by Isoniazid with positivity to epicutaneous test, suggesting both the implication of a type IV mechanism of immunologic hypersensitivity and the drug-induced toxicity. Further research is needed to find the underlying mechanisms of this type of reactions.



Figure 1 Epicutaneous test positive to Isoniazid.

References

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